

SULPHARSPHENAMINE: INDICATIONS FOR ITS USE AND TECHNIC FOR INTRAMUSCULAR INJECTION

By IRWIN C. SUTTON *

Sulpharsphenamine is probably as active as neoarsphenamine when given in large doses, but only small doses (0.4 gm.) may be given in the muscles. It is very toxic in the abortive treatment of syphilis, and when large amounts are administered.

Purpura and peripheral neuritis do not seem to be as common following intramuscular injection as when the intravenous route is used.

When the drug is given correctly into the muscles severe reactions are few, but cysts may form in spite of all precautions.

Cutaneous reactions are frequent and must be guarded against to the utmost. This may or may not be due to the concomitant use of mercurial inunctions.

Herxheimer reactions, probably due to the slow absorption of the drug, are rare, especially where a gradual introduction to treatment is made.

DISCUSSION by Harry E. Alderson, San Francisco; Samuel Ayres, Jr., Los Angeles; Howard Morrow, San Francisco; A. Edward Roome, Los Angeles.

SULPHARSPHENAMINE is a formaldehyde bisulphite preparation of arsphenamine base. It is similar to neoarsphenamine, but according to For-dyce, Rosen, and Myers, differs chemically in its action toward dyes and in its oxygen content. Like neoarsphenamine, it also varies greatly in its composition, but is more stable both in and out of solution and has the important property of being tolerated by the muscles when injected intramuscularly by a correct technic.

This drug was a forerunner of neoarsphenamine, but was rejected by Ehrlich in favor of the latter, chiefly because of the lower activity and higher toxicity of sulpharsphenamine. The French prepared a product called sulpharsenol about 1918 which was investigated by Voegtlin in 1922. It was finally found that the American and foreign products were practically identical. The present status of this drug seems to be below not only arsphenamine but also neoarsphenamine in tolerability and trypanocidal action.

The chief advantage of sulpharsphenamine is that the drug may be given into the muscles. This is important for the physician who is not adept at venipuncture, particularly in infants and those patients with inaccessible veins. Intramuscular injection automatically removes those early or nitritoid reactions, due to the sudden administration directly into the circulation of powerful drugs. R. L. Sutton has for years practiced the intramuscular injection of old salvarsan in concentrated solution. Like Craig, he believes that "one intramuscular injection is worth two intravenous injections." The advantages of intramuscular injection may be summed up as follows: a slower absorption with more prolonged action on the infection, avoidance of early reactions, a simplified technic, and the fact that it may be used where venipuncture is difficult or hazardous.

The chief drawbacks are pain, either slight or severe, and the formation of cysts and painful nodules.

In early syphilis, abortive treatment with large and frequent doses of sulpharsphenamine is distinctly hazardous. The treatment usually carried out consists of an intramuscular injection of 0.4 gm. sulpharsphenamine every three days until three injections have been given; then one every five days until five more injections have been given. The mercurial inunctions are started with the third injection and continued until thirty are taken at the rate of six a week. Under this combined therapy, Stokes and Behn found that the spirochetes rapidly disappeared from the early lesions and that healing was prompt.

In latent and all late stages of syphilis the drug may be given every five days for a series of six to eight injections, depending on tolerance, and individual indications, with mercury in the form of inunctions. I have found the "clean inunction" method of Cole very useful in securing the co-operation of the patient in this procedure.

In central nervous system syphilis, sulpharsphenamine may be used before resort to the special procedures of spinal drainage, intraspinal administration of fortified and unfortified blood-serum and intravenous injections of tryparsamide. The early reports on sulpharsphenamine by Voegtlin and others as to its potency in neurosyphilis have not been confirmed.

In pregnancy the dose should be cut in half and mercury administered very cautiously if at all. For the treatment of infantile syphilis sulpharsphenamine is of great value, as shown by Boone and Welch. Crawford and Fleming of Glasgow, however, found its action, as judged by Wassermann tests, inferior to arsphenamine and neoarsphenamine, but the symptomatic results in congenital syphilis remarkable. Infants stand treatment with sulpharsphenamine very well and with but little reaction to the injections. The dosage should be about 15 to 20 mg. per kilogram of body weight. Mercurial ointment may be easily applied under the binder.

In cardiovascular syphilis and in acute syphilitic processes in structures where it is imperative not to produce a Herxheimer reaction, sulpharsphenamine may be used cautiously following preliminary treatment with iodids and mercury.

This preparatory treatment should consist of one or two weeks with rest in bed if necessary; potassium iodid in doses of five drops, gradually increased to fifty, three times a day, and daily intramuscular injection of $\frac{1}{4}$ gr. mercury succinimide. Then intramuscular injections of sulpharsphenamine, starting with 0.2 gm. and increasing to 0.4 gm. every five days may be given and the mercury inunctions substituted for the injections.

While the statement appears on the ampule that sulpharsphenamine may be given subcutaneously, the pain and danger of sloughing precludes this method in my experience.

The essence of the technic for intramuscular injection consists in the dilution of the drug, and the amount of drug used. Following the suggestion of Claude Behn, I use three drops of sterile tap water for each decigram of the drug, and never inject more than 0.4 gm. and preferably 0.3 gm.

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Following the outline of epifascial injection technique given by J. H. Stokes, I have very few local reactions. This consists briefly of the following points:

With the patient lying prone with the toes in, the heels pointing out, the buttock is pulled down and the injection made by a quick down stroke with a long slender needle into the upper outer quadrant of the hip. The needle should slant slightly downward and inward. A bubble of air is injected on the top of the fluid, which acts as an air trap and, with the sliding of the muscles on their release, and the use of a slender needle, effectively prevents a backflow of the drug into the subcutaneous tissues along the needle tract. This leaking along the needle tract is the most common cause of painful indurations under the skin. I usually advise my patients to take a walk or climb stairs, for the exertion seems to help absorption and shortens the discomfort. It will be found that muscular and well developed people will stand the injections best; obese and nervous thin patients tolerate them but poorly.

TOXIC AND UNTOWARD EFFECTS

The complications of sulpharsphenamine treatment resolve themselves into those due to the deposition of an irritating drug in the tissue and those due to the inherent toxicity of the drug itself.

Painful reactions are not infrequent without the formation of nodules. These usually disappear with a sedative, hot sitz bath, or application of a heat lamp to the buttock. The nodular reactions are more lasting and may require repeated hot applications before they leave. Several times, on aspirating before injection, I have drawn up chocolate-colored fluid into the syringe from an old cyst. These cysts may not be seen on the surface, and only discovered by deep palpation. They are usually painless and their presence unknown to the patient. Abscess formation is practically unknown, but has been reported in obese patients. This was probably due to the deposition of the drug in the fatty tissue by too short a needle.

Peacock and Stokes and Behn have reported purpuric spots on the skin and mucous membranes after the intravenous use of sulpharsphenamine, but I have never known it to follow the intramuscular injection.

Belding noted a high incidence of peripheral neuritis in his patients who received large doses at frequent intervals. This is a serious objection, but does not seem to occur very often following intramuscular injection.

Erythrodermias following the use of sulpharsphenamine are very common when large doses are given directly into the veins. In combination with inunctions of mercury the intramuscular injection of the drug also gives a high percentage of cutaneous reaction.

Thus in the abortive treatment for syphilis three out of five patients developed a rather severe generalized dermatitis when the inunctions were started, after the third injection.

One man who had been saturated with cacodylates was put on sulpharsphenamine intramuscularly

for nonspecific treatment. Four hours after his first injection he had to scratch his feet because of the intense itching. He was promptly relieved by the intravenous injection of 1.0 gm. of sodium thiosulphite and atropine by mouth. He was alkalinized with soda bicarbonate, and another injection given three weeks later. Next day, over the site of the injection, there was a large area of confluent urticarial wheals with scattered papules over the body.

An elderly man with cardiovascular syphilis was given mercury by inunction and small injections of sulpharsphenamine weekly after a thorough preparation. After his fourth injection he noticed some itching, but said nothing about it. After his fifth, he presented acute generalized edema of the skin with extreme itching. He was given soda by mouth, large doses of thiosulphite into the veins, and drastic catharsis. However, this did not prevent him from having a typical attack of dermatitis exfoliativa, although the duration was only about two weeks.

DISCUSSION

HARRY E. ALDERSON, M. D. (490 Post Street, San Francisco)—Sutton's description of intramuscular technique is instructive and interesting. As he states, the chief advantage in the use of sulpharsphenamine is in its availability for intramuscular injection. Unfortunately there are occasional cases where intravenous therapy cannot be administered. It is in these cases and in congenital syphilis that the drug is particularly useful. Sutton calls attention to untoward effects. It is true that even with good technique painful persistent nodules or cysts develop occasionally. However, it seems to be safer and more free from bad after-effects than the other arsphenamines given intramuscularly.

When this drug first came out we tried it in the Stanford skin and syphilis clinic by the intravenous route. We treat there about 150 cases of syphilis weekly, so the drug was given a fair trial. We had to abandon its use intravenously, for most of our patients were upset and many of them very much so. Severe persistent vomiting was the principal symptom. There were no fatalities, however. From our experience we concluded that it was therapeutically inferior to the other arsphenamines, and for this reason, and also on account of the severe reactions produced, was not desirable for intravenous administration, but it had certain value as a spirochaeticide by intragluteal injection.

SAMUEL AYRES, JR., M. D. (Westlake Professional Building, Los Angeles)—I have had very little occasion to use sulpharsphenamine. In the few cases in which I have, it was given intravenously without harmful effects. I have seen two cases of dermatitis exfoliativa, resulting from the intramuscular administration of sulpharsphenamine. I do not see the necessity of using the intramuscular route, even in very young infants. An adequate dose of neoarsphenamine for an infant can be dissolved in one or two cubic centimeters of water and can be injected very easily into one of the scalp veins, especially on the side of the head or in the middle of the forehead.

When the baby cries, as it inevitably does under such circumstances, the veins are distended and no tourniquet is needed. The injection is made, using a hypodermic needle and a 2 cc. syringe.

HOWARD MORROW, M. D. (484 Post Street, San Francisco)—Sulpharsphenamine is a valuable addition to the other arsphenamines. It cannot replace arsphenamine or neoarsphenamine, but when intramuscular arsenical medication is indicated it is the preparation of choice. When given intramuscularly it is less painful than neoarsphenamine and has many advantages over the older arsphenamine preparations. Many investigators claim that sulpharsphenamine is of greater value in cerebrospinal syphilis or neurosyphilis in general.

Its value in hereditary syphilis cannot be questioned. When intramuscular arsenical medication is indicated we

give sulpharsphenamine weekly for ten injections, and for adults the dose should be 0.6 grams each.

A. EDWARD ROOME, M. D. (Medico-Dental Building, Los Angeles)—In my opinion sulpharsphenamine has a very definite place in therapy, and after a thorough trial of this drug at my clinic I have come to the same conclusion as to its value as mentioned by Alderson.

There is no doubt that its use intramuscularly is the ideal way of administering the drug on account of the slow absorption and its practical freedom from nitroid reactions.

DERMATOLOGY AS MEDICAL SCIENCE, HEALING ART AND PRACTICE OF MEDICINE †

By MOSES SCHOLTZ *

THE dermatologist engaged in unraveling and solving the diagnostic and therapeutic problems of individual patients hardly ever pauses long enough to survey the field of dermatology as a whole. Yet a study of dermatological research, of its possibilities and limitations; of the evolution of dermatology as a science; and the analysis and study of the relationship of the component units of dermatologic thought—morphology, histopathology, and pathogenesis is of great value and interest.

Besides the purely abstract and academic aspects of the subject, many practical problems of dermatology invite study, such as the relationship of dermatology to general medicine and to other specialties and the establishment of proper boundaries between them; the teaching of dermatology to undergraduates and graduates; the organization of dermatologic service in hospitals and clinics; the statistical survey and study of skin diseases, the analysis of dermatologic literature, cosmetic dermatology, dermatologic quackery, etc.

WHAT IS DERMATOLOGY?

The generally accepted definition is simple and implies the study and care of all diseases and lesions of the skin. But the establishment of the strict boundaries of dermatology from other branches of clinical medicine is not so easy, since skin lesions often develop as passing, incidental and minor symp-

toms of various more general diseases. The dermatologist is interested in them from the diagnostic point of view only.

Trophoneurotic or vasomotor dermatoses, such as Raynaud's disease, trophoneurotic ulcers and degenerations are described and treated simultaneously in manuals of dermatology, surgery, neurology, and medicine. It is my belief that dermatology should comprise any and all skin lesions, whether they are big and lasting enough to constitute independent dermatologic entities or are merely an incidental symptom of systemic affection. In the latter case the lesions should be accorded a proper place in the morphologic classification.

DERMATOLOGY VERSUS GENERAL MEDICINE

Because of the enormous frequency of skin lesions as manifestations of systemic conditions, only a very small fraction of the grand total of patients with skin lesions reach dermatologists; as a rule, only those that present diagnostic or therapeutic difficulties. The overwhelming majority of patients with skin lesions are treated by general practitioners, pediatricians, surgeons, and radiologists. Yet practitioners frankly admit their inadequate knowledge of diseases of the skin. The peculiar lack of interest in and disregard for dermatology as a specialty of medicine, in my opinion, is due to the defective methods of teaching dermatology.

This situation brings to dermatologists an all-important duty of restoring the interest and esteem of the general profession to his specialty. Some practitioners consider dermatology rather detached from the general subject of medicine, the understanding of which can be acquired only by an accumulated experience of many years.

It is my experience that the general practitioner, if demonstrated the rational methods of differential diagnosis, quickly grasps the idea that dermatologic diagnosis is more than an empirical product of individually accumulated experience, and he begins to enjoy the intellectual process of arriving at diagnosis through the correct principles and technique of differentiation.

DERMATOLOGY AS SCIENCE

The analytical study of the resources and limitations of dermatology as a medical science is a fascinating but insufficiently clarified problem. Some of the fundamentals may be deduced from the analysis of the skin as a subject of study. The skin being located on the surface of the body is subject to direct examination. This unique diagnostic and therapeutic opportunity explains why the inspection plays such a dominant part in dermatologic diagnosis. The extensive area occupied by the skin and the possibility of innumerable variations in localization, distribution, grouping and shape of lesions, makes for the steady growth of morphology as a paramount factor in dermatologic diagnosis.

The technical ease and impunity with which a biopsy can be performed has led to the development of another important diagnostic method—the histopathologic examination. This dual morphologic and histopathologic basis of the dermatologic

† Chairman's address, Section on Dermatology and Syphilis, presented at meeting of California Medical Association, Oakland, California, May 1, 1926.

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